Impaired Left Ventricular Functional Reserve in Hypertensive Patients With Left Ventricular Hypertrophy

Julio F. Tubau, Jadwiga Szlachcic, Shimon Braun, and Barry M. Massie

To determine whether patients with hypertension and especially those with left ventricular hypertrophy have subtle changes in cardiac function, we measured the increase in left ventricular ejection fraction and in systolic blood pressure to end-systolic volume index ratio with exercise in 40 hypertensive patients and 16 age-matched normotensive volunteers. Twenty-two hypertensive patients without hypertrophy had normal end-systolic wall stress at rest and exercise responses. In contrast, the 18 patients with echocardiographic criteria for left ventricular hypertrophy demonstrated a significant increase in end-systolic wall stress at rest compared with normal subjects (69 ± 16 vs. 55 ± 15 10^3 dyne/cm², p < 0.05) despite having normal resting left ventricular size and ejection fraction. In patients with left ventricular hypertrophy, the increase in ejection fraction with exercise was less than in the normotensive control subjects (7 ± 7 vs. 12 ± 8 units, p < 0.05), and Δ systolic blood pressure to end-systolic volume with exercise was reduced (3.3 ± 3.8 vs. 8.3 ± 7.7 mm Hg/ml/m², p < 0.05). The hypertensive patients with hypertrophy displayed a shift downward and to the right in the relation between systolic blood pressure to end-systolic volume ratio and end-systolic wall stress compared with control subjects and hypertensive patients without left ventricular hypertrophy. Thus, hypertensive patients with left ventricular hypertrophy by echocardiography and normal resting ejection fraction exhibit abnormal ventricular functional responses to exercise. This finding may have implications in identifying patients at higher risk for developing heart failure. (Hypertension 1989;14:1–8)

It has been long recognized that hypertension is associated with a high incidence of congestive heart failure, as well as other forms of cardiovascular morbidity and mortality.1,2 In particular, the presence of left ventricular hypertrophy (LVH) on the electrocardiogram increases the risk of developing congestive heart failure by almost 10-fold.2,3 From experimental and clinical data, it is suggested that LVH develops as a response to the increased load and, although initially adaptive, may finally lead toward heart failure.4 Early hemodynamic studies seemed to support this evolutionary change in left ventricular function in hypertension, but only the advent of echocardiography allowed a more complete study of ventricular function that included the measurement of afterload (i.e., end-systolic stress).4 Echocardiographic studies established that although some hypertensive (HTN) patients exhibited impaired fractional shortening, the majority maintained normal left ventricular function.5–8 Despite these observations, it is uncommon to witness the progression to heart failure in individual HTN patients. A potential explanation is perhaps the slow evolution of these changes as well as the beneficial effects of early detection and treatment of hypertension in prevention of heart failure.5

Previous studies by ourselves9 and others10 have demonstrated the presence of diastolic filling abnormalities in HTN patients with preserved systolic function and raise the possibility that these changes might be early indicators of compromised myocardial function. There is less consensus, however, regarding the presence of subtle early abnormalities of systolic function in these patients.5–8,11–14 The present study was undertaken to evaluate whether there is an impairment of the left ventricular functional reserve in HTN patients. This evaluation was accomplished by measurement of left ventricular systolic function at rest and during maximal supine bicycle exercise in a cohort of untreated HTN patients with or without LVH.

An important consideration in designing this study was to examine an age-matched group of control
subjects without hypertension and with a low probability of coronary artery disease because aging and coronary disease themselves may be characterized by structural and functional changes similar to those of long-standing hypertension.\textsuperscript{15,16}

Subjects and Methods

Patient Population

Male patients with essential hypertension who were free of other significant medical diseases were selected for the study. None had history of chest pain or any signs or symptoms suggesting congestive heart failure. Sixteen patients were untreated, and the remaining 24 had their antihypertensive medications withdrawn for at least 4 weeks before the study. Only those with supine diastolic blood pressures exceeding 95 mm Hg with less than 7 mm Hg variation on at least three consecutive visits were included.

Active asymptomatic men in the same age range as the hypertensive patients were recruited as control subjects from the community by advertisement. After giving written informed consent, both groups of subjects underwent treadmill exercise tests and exercise thallium-201 scintigraphy to exclude significant coronary artery disease. Echocardiography was performed for calculation of left ventricular mass and for exclusion of valvular and segmental wall motion abnormalities. This report represents a consecutive series of subjects who had normal exercise thallium-201 scintigrams and good quality echocardiograms and who were capable of performing supine bicycle exercise.

Echocardiography

M-mode and two-dimensional echocardiograms were performed by standard techniques in all subjects. M-mode measurements of left ventricular end-diastolic and end-systolic cross-sectional diameter and of interventricular septum and posterior wall thickness were made on three to five consecutive cycles with conventional criteria and were averaged.\textsuperscript{17,18} Left ventricular mass was calculated with the formula validated by Devereux\textsuperscript{19} and Reichek.\textsuperscript{20} Left ventricular mass index (LVMI) was obtained by dividing left ventricular mass by body surface area. Left ventricular meridional wall stress was calculated by the following formula: \[ WS = 1.332 \times P \times D / 4h(1 + h/D)^{1/3} \] dynes/cm\(^2\), where \( WS \) is wall stress, \( P \) is systolic blood pressure by cuff sphygmomanometry, \( D \) is the diameter, and \( h \) is mean wall thickness.\textsuperscript{21,22} To estimate the peak-systolic stress, the end-diastolic measurements were used, and for end-systolic stress, the end-systolic measurements were used.\textsuperscript{23}

Patients were considered to have LVH if their LVMI was two standard deviations above that of the normotensive subjects of similar age. This was determined by the confidence limits in our laboratory for the relation between LVMI and age in normal subjects (30–70-year range). All patients meeting this criterion had a posterior wall thickness of at least 1.1 cm. None of the studied patients had evidence of asymmetrical septal hypertrophy, valvular lesions, or segmental wall motion abnormalities.

Radionuclide Angiography

Left ventricular function was assessed by equilibrium blood pool radionuclide angiography at rest and during maximal supine bicycle exercise by use of a protocol described in detail previously.\textsuperscript{24} Briefly, after in vivo red blood cell labeling with technetium-99m radionuclide, angiographic studies were performed in the left anterior oblique projection that best separated both ventricles and the left ventricle from the left atrium. Scintigrams were obtained in list mode and reformatted into 20-msec frames that included only sinus beats within 10% of the average heart rate. These were obtained at rest and during the last 2 minutes of each stage of supine bicycle exercise. The exercise protocol consisted of 3-minute stages starting with free pedaling at 60 rpm. The workload was increased by 200 kiloponds/m/min every 3 minutes until a symptomatic end point of exhaustion was achieved. Heart rate was monitored continuously, and blood pressure was recorded noninvasively at the end of each stage with a calibrated sphygmomanometer.

Left ventricular ejection fraction (EF) was calculated by standard techniques after background subtraction. Left ventricular volumes were calculated by relating left ventricular counts to counts in a reference blood sample drawn during each scintigram with a count-based nongeometric technique as described previously.\textsuperscript{25} The EF response to exercise was considered abnormal if it did not increase by 5 units or if there was a decrease in patients with a resting EF equal to or greater than 70%.\textsuperscript{24,26}

Data Analysis

Exercise endurance and hemodynamic indexes at rest and during exercise were compared in normal subjects and in HTN patients with and without LVH. Left ventricular EF and the systolic blood pressure to end-systolic volume index ratio (SBP/ESVI) at rest and at maximum exercise were used as indexes of left ventricular function.\textsuperscript{27–29} The changes in these indexes from rest to maximum exercise were used to assess the exercise response. Age, the degree of LVH, and the calculated end-systolic wall stress were related to exercise performance in HTN patients and in normal subjects. Statistical analysis was performed by analysis of variance techniques; intergroup differences were detected by the Newman-Keuls test. All data is shown as mean\(\pm\)1 SD unless otherwise indicated.

Results

Patient Characteristics

The characteristics of the study population are summarized in Table 1. The 40 HTN patients were divided in two groups: the 22 patients without LVH were labeled HTN-no LVH, and the remaining 18
TABLE 1. Characteristics of the Study Population

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean age (yr)</th>
<th>Range (yr)</th>
<th>SBP (mm Hg)</th>
<th>DBP (mm Hg)</th>
<th>HR (beats/min)</th>
<th>LVMI (g/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>56±7</td>
<td>35–70</td>
<td>123±13</td>
<td>81±5</td>
<td>59±8</td>
<td>97±18</td>
</tr>
<tr>
<td>Hypertensive</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HTN-no LVH</td>
<td>54±10</td>
<td>35–66</td>
<td>154±17*</td>
<td>98±7*</td>
<td>68±10</td>
<td>93±10</td>
</tr>
<tr>
<td>HTN-LVH</td>
<td>55±9</td>
<td>40–69</td>
<td>162±20*†</td>
<td>102±6*</td>
<td>65±11</td>
<td>128±23†</td>
</tr>
</tbody>
</table>

SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; LVMI, left ventricular mass index; HTN-no LVH, hypertensive patients with no left ventricular hypertrophy; HTN-LVH, hypertensive patients with left ventricular hypertrophy.

*p<0.01 vs. controls.
†p<0.01 vs. HTN-no LVH.

patients who met the previously described criterion for LVH were defined as the HTN-LVH group. The race distribution was similar with 50% blacks among the HTN-LVH group and 39% blacks among the HTN-no LVH group.

There were no significant differences in the previous antihypertensive therapy or its duration between patients with or without LVH. Thirty-two and 44% of HTN-no LVH and HTN-LVH, respectively, had received two drugs usually consisting of a β-blocker and a diuretic, and the remainder of the two groups had been treated with single drug therapy. The duration of treatment varied from 6 months to 4 years with a median of 2½ years.

The 16 normal subjects chosen to provide a control group of similar age to the HTN patients were derived from a larger group of 37 (range 23–76 years) by limiting the age range (35–70 years) so that it matched that of the HTN patients. Their mean age was 56±7 years; all had normal systolic and diastolic blood pressures, and their mean LVMI was 97±18 g/m². Both patient groups had higher blood pressures than the control subjects. By definition, left ventricular mass was higher in the HTN-LVH than HTN-no LVH group, and only the former was significantly higher than that of the control subjects.

Exercise Performance

Exercise capacity was estimated by the maximum workload achieved on the supine bicycle ergometer (Table 2). The maximum workload achieved declined insignificantly with age in control subjects (r=−0.30, p=0.07) and significantly in HTN patients (r=−0.39, p<0.01). Both HTN-no LVH and HTN-LVH patients exercised to lower workloads compared with the normal group. However, there were no differences in maximum workload between HTN patients with and without LVH (Table 2).

Exercise heart rate declined with age in normotensive subjects (r=−0.55, p<0.01) but not in HTN patients (r=−0.13, p=NS). The HTN-LVH patients achieved lower exercise heart rates compared with control subjects and the HTN-no LVH group (118±20 vs. 131±16 and 135±18 beats/min, respectively, both p<0.05).

Exercise systolic and diastolic blood pressures were significantly higher in HTN-LVH and HTN-no LVH patients than in the normotensive control subjects. The pressure-rate product, an index of exercise cardiac workload, was higher in HTN-no LVH compared with HTN-LVH patients, but there were no differences between the HTN-LVH patients and the normotensive subjects.

Left Ventricular Function at Rest and During Exercise

The rest and exercise left ventricular function measurements are shown in Table 3. The resting EF was by definition normal (>50%) in the control subjects. The EF response to exercise was normal

TABLE 2. Exercise Performance

<table>
<thead>
<tr>
<th>Group</th>
<th>Workload (kiloponds/min)</th>
<th>Max HR (beats/min)</th>
<th>Max SBP (mm Hg)</th>
<th>Max DBP (mm Hg)</th>
<th>PRP (×10³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>975±233</td>
<td>131±16</td>
<td>189±21</td>
<td>85±8</td>
<td>24.7±4</td>
</tr>
<tr>
<td>HTN-no LVH</td>
<td>773±251*</td>
<td>135±18</td>
<td>213±15*</td>
<td>115±8*</td>
<td>28.9±5*</td>
</tr>
<tr>
<td>HTN-LVH</td>
<td>694±239*</td>
<td>118±20*†</td>
<td>205±21*</td>
<td>115±8*</td>
<td>24.2±5†</td>
</tr>
</tbody>
</table>

HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; PRP, pressure-rate product; HTN-no LVH, hypertensive patients with no left ventricular hypertrophy; HTN-LVH, hypertensive patients with left ventricular hypertrophy.

*p<0.05 or below vs. normotensive control subjects.
†p<0.05 vs. HTN-no LVH.
The hemodynamic response to exercise was also who had normal exercise EF responses (LVH1), patients increased their EF to a lesser extent than the normal subjects (64±10 to 71±11%), and their rest and exercise EF responses. The HTN-LVH 77 ±7%). All HTN-no LVH patients had normal in the control group (mean increase from 65±8 to 77±7%). All HTN-no LVH patients had normal rest and exercise EF responses. The HTN-LVH patients increased their EF to a lesser extent than the normal subjects (64±10 to 71±11%), and their exercise EFs were significantly lower than those of the control patients (71±11 vs. 77±7%, p<0.05). Among the 18 LVH patients, there were 12 patients who had normal exercise EF responses (LVH1), and six patients who had abnormal exercise EF responses (LVH2). To further evaluate the significance of these differences, the two subgroups (LVH1 and LVH2) were analyzed separately.

The LVH2 patients tended to be older (59±8 vs. 54±8 years, p=NS) and had a greater LVMI than LVH1 patients (145±31 vs. 121±8 g/m², p<0.05). The hemodynamic response to exercise was also different in the two LVH subgroups; exercise systolic blood pressures rose to higher levels in the LVH2 patients (223±15 mm Hg) than in the LVH1 subgroup (196±17 mm Hg) or HTN-no LVH patients (209±16 mm Hg, both p<0.05). The maximum heart rate response to exercise was similar in LVH1 and LVH2 subgroups (120±20 and 125±18 beats/min, respectively) but lower than in HTN-no LVH patients (135±18 beats/min).

The different responses of EF to exercise among LVH patients could be attributed primarily to a lesser decline of end-systolic volume during exercise. Indeed, the end-systolic volumes at the end of exercise were significantly greater in the LVH patients compared with normal subjects and HTN-no LVH patients (45±18 vs. 33±14 and vs. 37±18 units, both p<0.05). This difference was even more pronounced in the LVH2 patients (Table 3).

**Systolic Blood Pressure/End-Systolic Volume Ratio at Rest and During Exercise**

Because the LVH2 subgroup with a reduced EF response to exercise had higher systolic pressures and end-systolic volumes compared with the other groups and because changes in the SBP/ESVI ratio with varying loads provide an index of contractility, we examined the SBP/ESVI ratio itself and its change with exercise as a measure of cardiac performance and functional reserve. Despite the higher systolic blood pressures in HTN patients, the ratio was not statistically different among all groups at rest (Table 3). During exercise, however, the increase of the ratio (Δ) was less in the overall LVH group compared with control subjects (3.3±3.8 vs. 8.3±7.7 mm Hg/units/m², p<0.05). The LVH2 subgroup in particular, despite having the highest systolic blood pressures during exercise, failed to increase their SBP/ESVI ratio with exercise due to a comparatively greater increase in end-systolic volume (Table 3).

**Peak and End-Systolic Wall Stress at Rest**

Left ventricular afterload is largely determined by wall stress, and the inverse relation between EF and wall stress has been well documented.21-22 This relation was also present in our patients (r = −0.49, p<0.001).

Peak wall stress was not different among the groups of normal and HTN subjects. End-systolic wall stress, however, was significantly higher in LVH patients compared with normal subjects and HTN patients without LVH (69±16 vs. 55±15 and 57±15 10³ dynes/cm², both p<0.05, respectively), and it was highest in the LVH2 patients who did not normally increase their EF with exercise (Figure 1).

**Exercise Performance and Left Ventricular Mass**

There was an inverse relation between LVMI and the following indexes of left ventricular performance: exercise EF, ΔEF, exercise SBP/ESVI, and ΔSBP/ESVI. However, only ΔSBP/ESVI and ΔEF remained significantly related to LVMI when the correlations were performed in HTN patients alone. The interdependence between LVMI and these two indexes of exercise performance remained significant only in HTN patients when age was introduced in a stepwise multiple regression model (Table 4).
FIGURE 1. Bar graphs showing peak and end-systolic wall stress values at rest for various groups. NLS, normotensive subjects; LVH1, patients with left ventricular hypertrophy with normal exercise ejection fraction; LVH2, patients with left ventricular hypertrophy with abnormal exercise ejection fraction; HTN-no LVH, hypertensive patients without left ventricular hypertrophy. LVH2 patients with an abnormal ejection fraction response to exercise had the highest end-systolic wall stress.

Exercise Performance and End-Systolic Wall Stress

There was a significant inverse relation between end-systolic wall stress at rest and ΔSBP/ESVI in both normal subjects and HTN patients (r = −0.48, p < 0.01). ΔEF, on the contrary, was unrelated to end-systolic wall stress (r = −0.16, p = NS).

The HTN-no LVH patients were not different from their age-matched normotensive subjects with regard to ΔSBP/ESVI or end-systolic stress. The LVH patients, however, had significantly higher end-systolic wall stress and lower ΔSBP/ESVI values. This shift downward and to the right in the LVH patients was greater in the LVH2 subgroup, which was clearly separated from age-matched normotensive subjects and HTN-no LVH patients.

The LVH1 patients, who otherwise had normal EF response to exercise, exhibited mild increases in end-systolic wall stress and reductions in ΔSBP/ESVI compared with normotensive subjects and HTN-no LVH patients, although these differences were not statistically significant (Figure 2).

Influence of Previous Therapy

To eliminate the potential influence of previous antihypertensive therapy on our findings, we examined our results in 16 patients who had never been treated before.

The untreated LVH patients (n = 8) had higher end-systolic stress (69 ± 16 vs. 48 ± 7 dyne/cm², p < 0.01) and tended to have reduced the ΔSBP/ESVI compared with untreated HTN-no LVH patients (3.6 ± 3.6 vs. 8.1 ± 6.1, p = NS). These differences were again related to greater end-systolic volumes during exercise in LVH patients (49 ± 18 vs. 32 ± 14 units, p < 0.05). Although there were no statistical differences between the groups, two LVH patients displayed an abnormal EF response to exercise. Among patients previously treated, end-systolic wall stress was higher in those with LVH (70 ± 15 vs. 62 ± 16 dyne/cm², p = NS), and ΔSBP/ESVI was lower compared with HTN-no LVH patients (2.9 ± 3 vs. 5.4 ± 4, p = NS). There were no significant differences in either end-systolic stress or ΔSBP/ESVI among treated and untreated LVH patients.

Discussion

The high incidence of congestive heart failure in HTN patients with LVH has provoked considerable

### TABLE 4. Left Ventricular Mass Index and Exercise Performance

<table>
<thead>
<tr>
<th></th>
<th>Univariate correlations*</th>
<th>Multiple regression*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All patients</td>
<td>HTN</td>
</tr>
<tr>
<td>Exercise EF</td>
<td>−0.34†</td>
<td>−0.20</td>
</tr>
<tr>
<td>ΔEF</td>
<td>−0.40‡</td>
<td>−0.40‡</td>
</tr>
<tr>
<td>Exercise SBP/ESVI</td>
<td>−0.28†</td>
<td>−0.25</td>
</tr>
<tr>
<td>ΔSBP/ESVI</td>
<td>−0.42‡</td>
<td>−0.40‡</td>
</tr>
</tbody>
</table>

LVMI, left ventricular mass index; HTN, hypertensive patients; EF, ejection fraction; SBP/ESVI, systolic blood pressure to end-systolic volume index ratio.

*Univariate correlations value tabulated is regression coefficient r; multiple regression value tabulated is partial regression coefficient β.

†p < 0.01.
‡p < 0.001.
§p < 0.05.
patients with left ventricular hypertrophy. Results shown

Takahashi et al.36 showed impaired contractile per-

sive patients without left ventricular hypertrophy; LVH2, patients with

indexes, except in patients with more severe LVH

strated only minor abnormalities of systolic ejection

in experimental models of LVH and in humans, may cause subendocardial

systolic function reserve. Their findings range

...a transition between normal function and mi-

cardial insufficiency remains unclear. Some

flow or metabolic evidence of ischemia.31-32

Patients postulate that impaired coronary vascular

appears to be impaired.35

In most experimental models in which LVH

develops gradually, measurements of contractility

end-systolic wall stress at rest was also normal. The

significance of our normotensive population and selection bias

Exercise tolerance has been found to be reduced

with physiological aging.15 However, the small size of

have rarely demonstrated reduction in absolute

interest in the changes in left ventricular function

accompanying hypertrophy. The mechanisms respon-

sible for the transition between normal function and

myocardial insulinufficiency remain unclear. Some

authors postulate that impaired coronary vascular

reserve, which is common in experimental models of

and in humans, may cause subendocardial ischemia during periods of stress such as during

exercise.30-33 Results of experimental studies, how-

ever, have rarely demonstrated reduction in absolute

flow or metabolic evidence of ischemia.31,32

In older spontaneously hypertensive rats after prolonged periods of pressure overload hypertrophy, cardiac

pumping ability with increasing volume loading appears to be impaired.35

Previous investigators examining systolic perform-

ance in cross-sectional studies in HTN patients have observed a variable incidence (0-17%) of a
decreased EF by echocardiography5,6; however, underlying coronary artery disease was not system-
atically excluded. Other investigators have demonstr-

ated only minor abnormalities of systolic ejection

indexes, except in patients with more severe LVH

and elevated end-systolic wall stress at rest.4,8,12-14

Takahashi et al36 showed impaired contractile per-

formance in severe LVH (mean left ventricular wall

thickness of 1.5 cm) that was indicated by a shift to

the right of the end-systolic stress-diameter rela-

tion during afterload manipulations. It should be

emphasized that the patient population chosen for

the present study had normal EF at rest and less

severe hypertrophy than those patients with impaired

systolic function of previous reports.

Exercise tolerance has been found to be reduced

with physiological aging.15 However, the small size of

our normotensive population and selection bias

may explain the less striking reduction we observed.

Nevertheless, other related continuous variables

like total exercise time (r = -0.40, p < 0.05) and

exercise heart rate (r = -0.50, p < 0.002) significantly

declined with age. Exercise performance has been

found to be impaired in hypertensive patients with

LVH or more severe hypertension in concordance

with our findings.37,38

The appropriateness of the left ventricular func-
tion response during exercise in HTN patients

remains controversial. Early hemodynamic studies

demonstrated a decrease in exercise cardiac output

particularly in severe or long-standing untreated

hypertension.30 Previously, some investigators have

used EF and its change with exercise to examine

ventricular function reserve. Their findings range

from no abnormalities in either resting EF or its

response to exercise, even in patients with LVH, to

a greater than 50% incidence of abnormal EF

responses, even in patients without hypertrophy by electrocardiogram.26,38-40 These studies, however,

either did not assess left ventricular mass by echo-
cardiography or failed to systematically exclude

coronary disease or antihypertensive therapy.26,38-40

The present study was designed to examine left

ventricular function at rest and during exercise in

HTN patients and to relate these findings to the

degree of LVH. We made a particular effort to

exclude hemodynamically significant coronary artery

disease by multiple noninvasive techniques and

used age-matched normotensive subjects to account

for age-related changes in LVH.26,38,39 In addition,

we excluded patients with severe LVH and overt

systolic dysfunction to focus on the early changes in

left ventricular function during exercise.

The present data show evidence of impaired left

ventricular function during exercise in patients with

LVH, manifested by a lesser increase in EF and

SBP/ESVI with exercise. LVH patients also had

higher resting and, in all likelihood, exercise left

ventricular end-systolic wall stress values. Con-

versely, patients without LVH had normal func-
tional responses during exercise, and their end-
systolic wall stress at rest was also normal. The

significant inverse relation between these indexes of

left ventricular function and left ventricular mass is

notable. These findings strongly suggest that

although hypertension alone does not adversely

affect left ventricular performance, functional reserve decreases as LVH progresses.

The peak SBP/ESVI ratio has been proposed as an

index of contractility that is less dependent on

afterload and preload than the EF.7-11 This index

has been applied to patients with valvular and

coronary artery disease both at rest23 and during

FIGURE 2. Plot demonstrating ventricular functional

reserve in various groups as indicated by relation between

changes in systolic pressure to end-systolic volume index

(△SBP/ESVI) ratio and end-systolic wall stress at rest.

NLS, normotensive subjects; HTN-no LVH, hyper-
tensive patients without left ventricular hypertrophy; LVH1,

patients with left ventricular hypertrophy with normal

exercise ejection fraction responses; LVH2, patients with

left ventricular hypertrophy with abnormal ejection frac-

tion responses. Note shift down and to the right in

patients with left ventricular hypertrophy. Results shown

represent mean±SEM.
maximal exercise$^{41,42}$ and has been thought to provide a better index of functional reserve.

Since exercise systolic blood pressure has been recognized as an important determinant of left ventricular mass in hypertension$^{43}$ and one of the determinants of the abnormal response to exercise is an increase in end-systolic volume, the usefulness of this index in the present study is not surprising. The ΔSBP/ESVI versus end-systolic stress relation proved to be better than any single parameter alone and better than the ΔEF versus end-systolic stress relation in separating normotensive subjects and HTN–no LVH patients from those with LVH. Furthermore, LVH1 patients with normal EF responses to exercise displayed a shift downward and to the right of their ΔSBP/ESVI versus end-systolic wall stress compared with control subjects and HTN–no LVH patients, although these differences did not achieve statistical significance. Because left ventricular functional reserve is in part influenced by resting systolic blood pressures,$^{29}$ it is conceivable that differences in baseline blood pressures or maximum workload achieved could have affected our results. However, plots of ΔSBP/ESVI versus baseline systolic blood pressure or workload (not shown) showed a downward shift of this relation in the HTN-LVH patients compared with HTN–no LVH patients.

**Limitations of the Study**

Systolic indexes of left ventricular function were not fully delineated by varying loading conditions. Thus, contractility was not assessed; rather, left ventricular functional reserve was characterized by single points at rest and during exercise. Furthermore, noninvasive systolic blood pressure was used in the place of end-systolic pressure. These measurements have previously been shown to correlate well and were used by others.$^{29,40,41}$

Another limitation is that the majority of our patients had been previously treated. Nevertheless, when the untreated patients were examined separately, the differences between HTN patients with and without LVH persisted, although the level of statistical significance was reduced.

**Conclusion**

These results indicate that subtle impairment in left ventricular functional reserve can be demonstrated in patients with chronic hypertension and LVH even when undergoing coronary artery disease and the effect of aging are removed. The exercise-induced increase in the SBP/ESVI ratio and its relation to wall stress appear to detect these changes in LVH patients relatively earlier than the exercise EF.

The mechanisms underlying these abnormal responses were not directly assessed in this study, and although they do correlate with LVH and end-systolic wall stress, it is uncertain whether this relation is causal. It is tempting, however, to hypothesize a component of endocardial ischemia based on the known impairment of coronary reserve in these patients with LVH and the observed elevated wall stress. Whether these patients will evolve toward overt heart failure or whether antihypertensive therapy and, even more important, treatment-induced reversal or prevention of progression of LVH will halt this unfavorable evolution can only be answered by prospective longitudinal studies.

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